CANCER AMONG FORMER EMPLOYEES OF THE JOHNS-MANVILLE ASBESTOS-CEMENT FACTORY IN WEST HILL, ONTARIO: AN UPDATED ANALYSIS AND ASSESSMENT OF RISK

Murray M. Finkelstein PhD, MDCM
Health Studies Service
Ontario Ministry of Labour

May 2, 1988

INDEX

Executive Summary .....Page 3
Introduction .....Page 6
The Study Population.....Page 7
Statistical Methods .....Page 9
Results .....Page 11
Discussion .....Page 31
References .....Page 33

EXECUTIVE SUMMARY

In 1947, the Johns-Manville Company opened a plant in West Hill, Ontario for the manufacture of rock wool insulation materials and asbestos-cement pipe. This plant, between 1947 and 1980, manufactured asbestos-cement pipe using a mixture of two kinds of asbestos: chrysotile and crocidolite. At various times during its existence, this plant also manufactured asbestos-cement construction board, using only chrysotile, and asbestos insulation materials, using a third kind of asbestos, amosite.

The employees of this factory have experienced a high incidence of lung scarring from the disease asbestosis, and have been at greatly increased risk of developing the asbestos-associated cancers mesothelioma, lung cancer, and gastrointestinal cancer. After reviewing the information on the health experience of these workers collected by the Health Studies Service of the Ministry of Labour, the Royal Commission on Matters of Health and Safety Arising From the Use of Asbestos in Ontario concluded that this factory was the scene of a 'world-class occupational health disaster'.

It is the purpose of the present report to update the investigation of the health experience of the 4729 workers in this population and to present an analysis of risk factors for asbestos-associated cancers in this workforce that might prove useful to those formulating criteria for the Compensation of asbestos diseases in the Johns-Manville population.

The present report updates the analysis of the cancer experience of this workforce to the end of 1985. The results of a cohort mortality analysis indicate that workers who were employed in jobs that did not involve exposure to asbestos and workers who did have exposure to asbestos but who were employed for less than one year had a cancer experience that was not substantially different from that of the general male population of Ontario. In contrast, men who worked in asbestos-exposed jobs and who were employed for one year or longer experienced an overall rate of death 50% higher than that of the general population and their cancer mortality rate

was tripled. There were 33 deaths due to malignant mesothelioma, with an average shortening of life of 15 years. The lung cancer mortality rate was tripled, with an average loss of life expectancy of 9 years, while the mortality rate due to gastrointestinal cancer was doubled, with an average loss of life expectancy of 7 years. There were no deaths from laryngeal cancer in the exposed members of this workforce.

Case-control methodology was used to investigate the association between the risk of developing lung or gastrointestinal cancers and a number of potential risk factors including asbestos exposure, age at hire, and year of hire. Detailed job histories have been collected for each worker and the results of air sampling surveys have been used to calculate quantitative asbestos-exposure profiles for each worker. These profiles were <u>not</u> used in the present analysis because the resources required to carry out the appropriate analyses were not available. As a substitute for these exposure profiles, the present analysis has used the length of time in asbestos-exposed jobs as the measure of asbestos exposure. It is known that the magnitude of exposure varied from job to job and that conditions changed with time. Length of time in exposed jobs is thus only a crude measure of asbestos "dose", but a simple measure, such as this one, is probably suitable for the development of criteria for the compensation of disease developing in these workers.

The cohort and case-control analyses indicated that no increase in lung or gastrointestinal cancer risk was detectable before 20 years from first employment. Risk was increased after a "latency" of 20 years and the length of time spent in asbestos-exposed jobs was a significant risk factor for both lung and gastrointestinal cancers. Compared to workers in unexposed jobs or workers who had worked for less than 1 year in exposed jobs, men who were exposed to asbestos from 1 to 10 years had a risk of cancer that was approximately doubled, while men who worked more than 10 years in exposed jobs had a risk of cancer that was increased approximately 5-fold. Only one of the cancer victims in the present analysis started work after 1960. It is known that conditions at the plant were

improved as the years passed, and it is probable that workers hired later than 1960 are at lower risk of cancer. It will not be possible to make an assessment of this hypothesis without a future update of this study.

Cancer victims were identified for the present analysis as a result of death from cancer or some other cause. It is possible that non-fatal cases of cancer have occurred in this workforce and were not recognized in this analysis. A search could be made for such individuals by linking the Johns-Manville roll of names with the records of the Ontario Cancer Treatment and Research Foundation.

Because of the risk faced by members of this workforce, it would be tempting to recommend medical surveillance in order to detect new cancers at as early a stage as possible. Regrettably, no screening procedure has been demonstrated to alter the mortality rates for mesothelioma, lung, or gastrointestinal cancers. The only action which is likely to prove beneficial, at this time, is smoking cessation. In 1983, the Health Studies Service mailed, to all members of the Johns-Manville population for whom an address could be located, an advisory recommending smoking cessation as a health protective measure. <u>It is recommended that, when the results of the present study are made public, the smoking advisory should be repeated and promoted.</u>

INTRODUCTION

In 1947, the Johns-Manville Company opened a plant in West Hill, Ontario for the manufacture of rock wool insulation materials and asbestos-cement pipe. This plant, between 1947 and 1980, manufactured asbestos-cement pipe using a mixture of two kinds of asbestos: chrysotile and crocidolite. At various times during its existence, this plant also manufactured asbestos-cement construction board, using only chrysotile, and asbestos insulation materials, using a third kind of asbestos, amosite.

The employees of this factory have experienced a high incidence of lung scarring from the disease asbestosis[1,2,3], and have been at greatly increased risk of developing the asbestos-associated cancers mesothelioma, lung cancer, and gastrointestinal cancer[4]. After reviewing the information on the health experience of these workers collected by the Health Studies Service of the Ministry of Labour, the Royal Commission on Matters of Health and Safety Arising From the Use of Asbestos in Ontario concluded that this factory was the scene of a 'world-class occupational health disaster'[5].

It is the purpose of the present report to: 1) update the investigation of the health experience of these workers, and, 2) to present an analysis of risk factors for asbestos-associated cancers in this workforce that might prove useful to those formulating criteria for the Compensation of asbestos diseases in this population.

The Study Population

A list of employees was collected from Company files and work histories were photocopied at the plant. The study population consists of the 4729 men for whom adequate information about name and date of birth were available to perform a mortality search at Statistics Canada.

The distribution of the dates of hire for the workers is given in Table 1.

TABLE 1: THE DISTRIBUTION OF YEAR OF HIRE

YEAR OF HIRE	NUMBER
HIRED FROM 1947-1955	1187
HIRED FROM 1956-1965	1057
HIRED FROM 1966-1975	1509
HIRED AFTER 1975	477
TOTAL	4729

Detailed job information was available in the work history, for most workers, and this data was used to classify each worker as "Exposed to Asbestos" or "Unexposed". Workers considered to have been unexposed were those who had worked in the Rockwool or Fibrous Glass operations, who had worked outdoors in shipping operations, or had worked at clerical jobs. Of the 4729 men in the cohort, 1563 were considered to have been unexposed and 3166 were classified as exposed.

Air sampling information was available from a number of surveys, and these data have been used in conjunction with the work histories to calculate personal exposure histories for each worker[4]. This detailed exposure data was not utilized in the present report because of a lack of resources.

As a surrogate for detailed exposure information, length of employment has been used as the exposure variable in this

report for the purpose of analyzing the health experience of the workforce with respect to exposure to asbestos. Gross Length of Employment has been calculated as the time interval between the date of hire and the date of termination. For some of the men, this length is an overestimate of the actual time employed because of breaks in employment, which are ignored in this calculation. There was a substantial amount of turnover in the Johns-Manville workforce. Fifty percent of the population had a gross length of employment of one year or less, 38% were employed between 1 and 10 years, and 12% were employed 10 years or more.

STATISTICAL METHODS

The vital status of each member of the Johns-Manville cohort was determined by submitting the list of names to Statistics Canada for a computerized linkage to a file of all deaths registered in Canada since 1950. A minimum probability for acceptability of a positive link was chosen and manual resolution of positive links was carried out making use of further information which is not available on the computerized Canadian Mortality Data Base. Follow-up terminated at the end of 1985, the last year currently available for computerized matching. It is possible that some deaths may have been missed by this tracing technique because of differences in the name and birth date recorded on the employment record and the death certificate, and because some workers may have died outside of Canada. It has been estimated that the number of deaths missed in the search is less than 10% of the total number of deaths[4].

The mortality experience of the Johns-Manville employees was compared with that of the general population of Ontario men by means of a Standardized Mortality Ratio (SMR) analysis. In this analysis, the number of deaths one would have expected to see in the Johns-Manville population was calculated by assuming that the Johns-Manville death rates would be identical to those of the general population of Ontario males, and by taking account of the ages and birthdates of the workers. After calculating the "EXPECTED" numbers of deaths for the various causes, the numbers actually "OBSERVED" were counted and the ratio OBSERVED/EXPECTED times 100 was computed. This ratio is known as the Standardized Mortality Ratio, or SMR. Because of chance fluctuations in the mortality pattern, the SMR might not be 100 even if there really is no underlying difference between the study group and the general population. The influence of chance fluctuations was assessed by comparing the observed pattern to the Poisson Statistical Distribution. The calculation of the SMRs and confidence intervals was performed using the "Person-Years" computer program written by Professor Julian Peto[6].

For those men dying of the various asbestos-associated

diseases, the number of years of life-shortening, or loss of life expectancy, was calculated as follows. The number of years of life expectancy remaining to each man at the date he was hired was determined from the statistics published in the Ontario Life Tables[7]. The loss of life expectancy was then computed as the difference between the predicted and actual lifespans.

A variety of statistical methods were used in the Case-Control Analysis. Comparisons of proportions were made using Fisher's Exact Test, the Chi-Square Test for Trend, and the Mantel-Haenszel Chi-Square Test as programmed in the statistics package True Epistat[8]. Unconditional Logistic Regression was performed using True Epistat, while Conditional Logistic Regression was carried out using the computer program PECAN[9].

RESULTS

A) THE COHORT ANALYSIS:

In this analysis, the mortality experience of the population of Johns-Manville employees was compared with that of the general population of Ontario men. In order to look for a pattern of risk associated with exposure to asbestos, 4 subgroups were formed. These groups were:

Group 1:	Unexposed.	Employed less than 1 year:	953 men
Group 2:	Exposed.	Employed less than 1 year:	1392 men
Group 3:	Unexposed.	Employed 1 year or more:	610 men
Group 4:	Exposed.	Employed 1 year or more:	1774 men

It would be expected that the mortality pattern in this workforce would vary with time. The reasons for this variation include the so-called "healthy-worker effect" and the delayed appearance of diseases caused by asbestos. The "healthy worker effect" is a phenomenon observed in most workforces. Since, generally speaking, it is the fit who are hired for factory jobs, the workforce will appear to be healthier than the general population for the first 10 or 15 years after hire since the general population includes individuals who are already sick or dying at the time that the factory worker is hired. It has also been found that diseases, such as asbestosis or cancer, caused by exposure to asbestos do not cause death until 15 or more years have elapsed from the time of first exposure. In order to allow for the changing pattern in time, the follow-up period has been subdivided into the intervals 1-10 years, 10-20 years, 20-30 years, and 30 or more years since the start of exposure, for the exposed workers, or since the start of employment for the unexposed.

The mortality pattern, for causes of death pertinent to asbestos exposure, is presented in Table 2. In this analysis the causes are classified according to the official death certificate codings. The Lung Cancer category includes 12 pleural mesotheliomas miscoded to the lung cancer code, while the Abdominal Cancers grouping (ICD 150-159) includes a number of peritoneal mesotheliomas (appropriately coded).

TABLE 2

MORTALITY RATIOS ACCORDING TO CAUSE OF DEATH(OFFICIAL CODINGS)
AND TIME FROM FIRST EXPOSURE OR EMPLOYMENT

YEARS SINCE FIRST EMPLOYMENT OR EXPOSURE

		1-10 YEARS			10-20 YEARS			20-30 YEARS			>30 YEARS			TOTAL > 20		
DIAGNOSIS	GROUP	OBS	EXP	SMR	OBS	EXP	SMR	OBS	EXP	SMR	OBS	EXP	SMR	OBS	EXP	SMR
ALL CAUSES	UNEXPOSED <1	15	15.8	95	15	21.1	71	36	28.8	125	13	18.1	72	49	46.9	105
ALL CAUSES	EXPOSED <1	26	27.7	94	37	41.9	88	55	49.5	111	23	29.8	77	78	79.3	98
ALL CAUSES	UNEXPOSED >1	7	15.6	45	24	26.7	90	28	36	78	20	20	100	48	56	86
ALL CAUSES	EXPOSED >1	27	41.8	65	57	75.4	76	125	88.5	141	58	35.9	162	183	124	**147**
ALL CANCER	UNEXPOSED <1	2	2.1	95	2	4.4	45	9	7.1	127	3	5.1	59	12	12.2	98
ALL CANCER	EXPOSED <1	5	4.1	122	9	8.8	102	9	12.5	72	5	8.3	60	14	20.8	67
ALL CANCER	UNEXPOSED >1	2	2.5	80	8	5.6	143	8	9	89	7	5.4	130	15	14.4	104
ALL CANCER	EXPOSED >1	3	6.6	45	10	16.3	61	62	22.9	271	30	10	300	92	32.9	**280**
LUNG CANCER	UNEXPOSED <1	1	0.4	250	2	1.1	182	5	2.4	208	3	1.9	158	8	4.3	186
LUNG CANCER	EXPOSED <1	1	0.9	111	3	2.6	115	4	4.4	91	4	3	133	8	7.4	108
LUNG CANCER	UNEXPOSED >1	0	0.6	0	0	1.7	0	2	3.1	65	2	1.9	105	4	5	80
LUNG CANCER	EXPOSED >1	2	1.5	133	6	5	120	30	8.1	370	9	3.8	250	39	11.7	**333**
ABDOMINAL	UNEXPOSED <1	0	0.6	0	0	1.3	0	0	2.2	0	0	1.5	0	0	4.7	0
ABDOMINAL	EXPOSED <1	0	1.1	0	3	2.7	111	1	3.9	26	1	2.5	40	2	6.3	30
ABDOMINAL	UNEXPOSED >1	1	0.8	127	5	1.8	272	2	2.8	71	2	1.7	121	4	4.6	87
ABDOMINAL	EXPOSED >1	0	1.9	0	0	5.1	0	12	7.1	169	9	3.0	300	21	10.1	**208**
GI CANCER	UNEXPOSED <1	0	0.4	0	0	0.9	0	0	1.6	0	0	1.05	0	0	2.65	0
GI CANCER	EXPOSED <1	0	0.9	0	2	2	100	0	2.8	0	1	1.7	59	1	4.5	22
GI CANCER	UNEXPOSED >1	1	0.6	167	3	1.4	214	2	2	100	1	1.1	91	3	3.1	97
GI CANCER	EXPOSED >1	0	1.4	0	0	3.7	0	9	5.1	177	5	2.1	238	14	7.2	**194**
NON-MALIGNANT DISEASES																
RESPIRATORY	UNEXPOSED <1	0	0.5	0	1	0.9	111	3	1.5	200	0	1.1	0	3	2.6	115
RESPIRATORY	EXPOSED <1	0	0.9	0	2	1.7	118	3	2.6	115	1	2	50	4	4.6	87
RESPIRATORY	UNEXPOSED >1	0	0.6	0	1	1.3	77	1	2.2	45	1	1.4	71	2	3.6	56
RESPIRATORY	EXPOSED >1	0	1.4	0	2	3.3	61	16	5	320	2	2.5	80	18	7.5	**240**
ASBESTOSIS	UNEXPOSED <1	0	0.02	0	0	0.04	0	0	0.07	0	0	0.04	0	0	0.11	0
ASBESTOSIS	EXPOSED <1	0	0.04	0	1	0.08	1250	0	0.12	0	0	0.07	0	0	0.19	0
ASBESTOSIS	UNEXPOSED >1	0	0.03	0	0	0.06	0	0	0.1	0	0	0.05	0	0	0.15	0
ASBESTOSIS	EXPOSED >1	0	0.06	0	1	0.16	625	6	0.22	2700	1	0.09	1100	7	0.31	**2260**
HEART	UNEXPOSED <1	3	2.7	111	3	7	43	12	10.7	112	6	6.5	92	18	17.2	105
HEART	EXPOSED <1	3	5.9	51	10	14.1	71	24	18.5	130	4	10.7	37	28	29.2	96
HEART	UNEXPOSED >1	3	4.1	73	6	10	60	11	13.8	80	4	7.2	56	15	21	71
HEART	EXPOSED >1	8	10.5	76	24	27.2	88	15	33.5	45	17	13	131	32	46.5	69

LEGEND: OBS=NUMBER OBSERVED. EXP=NUMBER EXPECTED. GI CANCER includes esophagus, stomach, and bowel.
In the TOTAL > 20 YEARS Column, the underlined SMRs are those for which $P < 0.05$.

There was little substantial difference between the mortality experiences of the Johns-Manville population and the general population of Ontario with the exception of those workers who had been employed more than 1 year and who had been exposed to asbestos. Those men experienced an overall mortality rate, in the period 20 or more years since first employment, that was 50% higher than that of the general population, and their risk of death from cancer was tripled.

For twelve deaths in which the cause of death was coded to Lung Cancer, the death certificate actually stated the cause of death to be Mesothelioma. There was 1 death in each of Groups 1, 2, and 3, and 9 deaths from Group 4. If one subtracts these cases from the appropriate columns of Table 2, the following revised SMR results are obtained:

TABLE 2a: LUNG CANCER SMRs CORRECTED FOR MISCODED MESOTHELIOMA

		YEARS FROM FIRST EXPOSURE					
		1- 20			20 OR MORE		
	GROUP	OBS	EXP	SMR	OBS	EXP	SMR
LUNG CANCER	UNEXPOSED <1	3	1.5	200	7	4.3	163
LUNG CANCER	EXPOSED <1	4	3.5	114	7	7.4	95
LUNG CANCER	UNEXPOSED >1	0	2.3	0	3	5	60
LUNG CANCER	EXPOSED >1	7	6.5	108	31	11.7	265

If one combines the unexposed men and the exposed men who worked for less than 1 year into a new subgroup called "Unexposed or Exposed for Less Than One Year", one obtains the following comparison for the lung cancer SMRs:

TABLE 3: A COMPARISON OF THE LUNG CANCER SMRs OF WORKERS EXPOSED TO ASBESTOS AND EMPLOYED FOR ONE YEAR OR MORE WITH THE SMRs OF WORKERS UNEXPOSED OR EMPLOYED LESS THAN ONE YEAR

	YEARS SINCE FIRST EXPOSURE					
	1- 20			20 OR MORE		
EXPOSURE CATEGORY	O	E	SMR	O	E	SMR
UNEXPOSED OR EXPOSED < 1 YEAR	7	7.4	95	17	16.7	102
EXPOSED WORKERS EMPLOYED > 1 YEAR	7	6.5	108	31	11.7	265

There is a substantial excess of lung cancer appearing 20 or more years after first exposure among men employed 1 year or more. In this analysis, there is no indication of increased risk of lung cancer in the workforce prior to 20 years from first exposure. In the interval 1-20 years from first exposure 7 cases of lung cancer were observed while 6.5 were expected. In the interval 15-20 years from first exposure, there were three deaths from lung cancer observed while 3.1 were expected.

In addition to lung cancer, the exposed workers were at substantially increased risk of death from gastrointestinal (esophagus, stomach, or bowel) cancer. In the period following 20 years from first exposure there were 7.2 cases expected, but 14 deaths were observed; this is a statistically significant excess ($P < 0.02$).

There were 33 deaths from mesothelioma in the cohort. Twenty-three were of the pleural type, 9 were peritoneal, and the pathology of one remains to be determined. Two of these deaths were among men who had been employed less than 1 year (one each from the exposed and unexposed categories) and 31 deaths were among men who had been employed more than 1 year (3 among men classified as unexposed and 28 among men classified as exposed). The cases of mesothelioma occurring among men without recorded work in asbestos-exposed jobs cannot be explained with certainty. They might be due to ambient

exposures in the plant environment, to unrecorded assignments in asbestos-exposed jobs, or to exposures either before or after employment at Johns-Manville.

The men dying of mesothelioma were younger than the men dying of lung or gastrointestinal cancers. The first death occurred 14 years after hire and the average age at death, of the men dying of mesothelioma, was 56 years while 27(82%) of the 33 men were less than 65 years of age at death. For men dying of lung or GI cancers, 15 or more years after start of employment or exposure, the mean ages at death were 62 and 65 years respectively. Fifty-seven percent of the men dying of lung cancer were less than 65 years of age, as were 47% of the men dying of GI cancers. The age distributions of the men dying of these malignancies are given in Table 4 and displayed graphically in Figure 1.

TABLE 4: THE AGE DISTRIBUTIONS OF THE MEN DYING OF CANCER

	AGE AT DEATH Number and Percent by Age				
CAUSE	40-50	50-60	60-70	70-80	TOTAL
MESOTHELIOMA	6(18%)	17(52%)	6(18%)	4(12%)	33
GASTROINTESTINAL	0	3(16%)	12(63%)	4(21%)	19
LUNG CANCER	3(6%)	18(34%)	23(43%)	9(17%)	53
TOTAL	8	38	41	17	105

AGES AT DEATH BY TYPE OF MALIGNANCY FOR ALL WORKERS IN THE STUDY

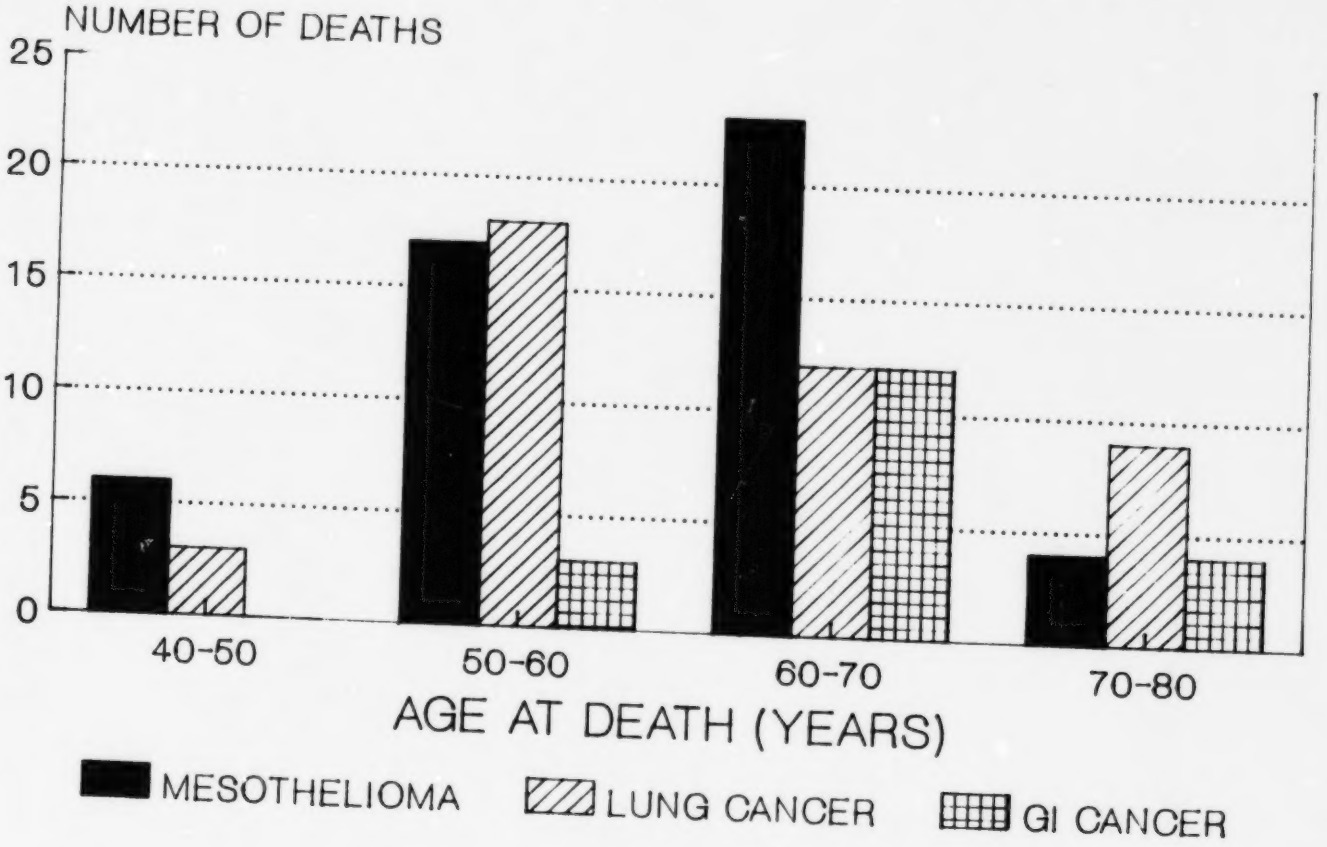


FIGURE 1

The average loss of life expectancy for the men dying of mesothelioma was 15.1 years, while for those dying of lung or GI cancers, 20 or more years after hire, it was 9.3 and 6.8 years respectively. The total loss of life expectancy was 499 years for men dying of mesothelioma. For men dying of lung or GI cancers 20 or more years after starting, the totals were 448 and 122 years. A substantial proportion of the years of life lost to asbestos disease in this population was thus due to death from mesothelioma.

Cancer of the larynx has occasionally been found to be associated with exposure to asbestos. There were 2 deaths of laryngeal cancer in the Johns-Manville population, of which only one was coded to this cause; 1.23 deaths of laryngeal cancer would have been expected in the workforce following 20 years from first exposure. Both of the men who died of laryngeal cancer were employed for less than 1 month and neither worked in asbestos-exposed jobs. No deaths of laryngeal cancer were observed among exposed workers; the expected number was 0.83 following a latency of 20 years.

THE CASE-CONTROL STUDY

The cohort analysis found that men with a Gross Length of Employment of one year or more, who had worked in jobs entailing exposure to asbestos, were at substantially increased risk of death from mesothelioma and lung and gastrointestinal cancers. In order to better define the risk factors for these diseases a case-control study was undertaken of lung and gastrointestinal cancers.

In a case-control study, the control individuals are randomly selected from the study population, and their exposures thus provide an estimate of the exposure pattern in the workforce. A comparison of the exposure patterns of the cases and controls then provides information about any association between exposure and the chance of being an individual who has developed the disease under study.

1) Identification of the Cases:

To identify cases of lung and GI cancer, use was made of all available information including the death certificate, pathology reports, autopsy reports, and histological reviews by the Canadian Tumour Reference Centre in Ottawa. Any man in whom one of these tumours had been identified was selected as a "CASE" irrespective of the certified cause of death. Since a worker must have died in order for this categorization to have occurred, it is possible that there were some non-fatal cases which have not been identified.

2) Lung Cancer:

There were 71 men in whom lung cancer was diagnosed either before death or from the examination of tissue after death. Each of these men was individually matched with 3 other members of the Johns-Manville population, using random numbers to ensure an unbiased selection process, and restricting eligibility to those potential matches who were still alive at the date of death of the case. The factors used in matching were year of birth and year of hire, and an attempt was made to match as closely as possible on these variables. Year of birth

was selected as a matching variable because risk factors such as cigarette smoking habit are known to vary with birth cohort. Year of hire was a matching variable because dust conditions in the factory were known to have changed over time, and because it was not planned to make use of the environmental measurements in the present analysis.

3) The measure of exposure:

The measure of exposure used in this analysis is the length of time spent working in asbestos-exposed jobs. To compute this measure, the work history of each study subject was coded for the computer and the number of days between the start and stop dates of each job was calculated. The number of years spent in asbestos exposure was then the sum of the number of days spent in all exposed jobs, divided by 365. Control subjects, who were still employed when their match died, ceased accumulating exposure at the date of death of their respective cases. In the present analysis no account is taken of the premise that exposure accumulated shortly before death is unlikely to be a causal factor in the development of cancer.

Figure 2 compares the lengths of exposure of the men dying of lung cancer, 20 or more years after first exposure, and of their control subjects. It can be seen that in comparison with the control subjects, there is a clustering of men with lung cancer in the longer asbestos exposure categories, suggesting an association between asbestos exposure and the risk of lung cancer.

THE LENGTHS OF EXPOSURE OF LUNG CANCER CASES AND CONTROLS

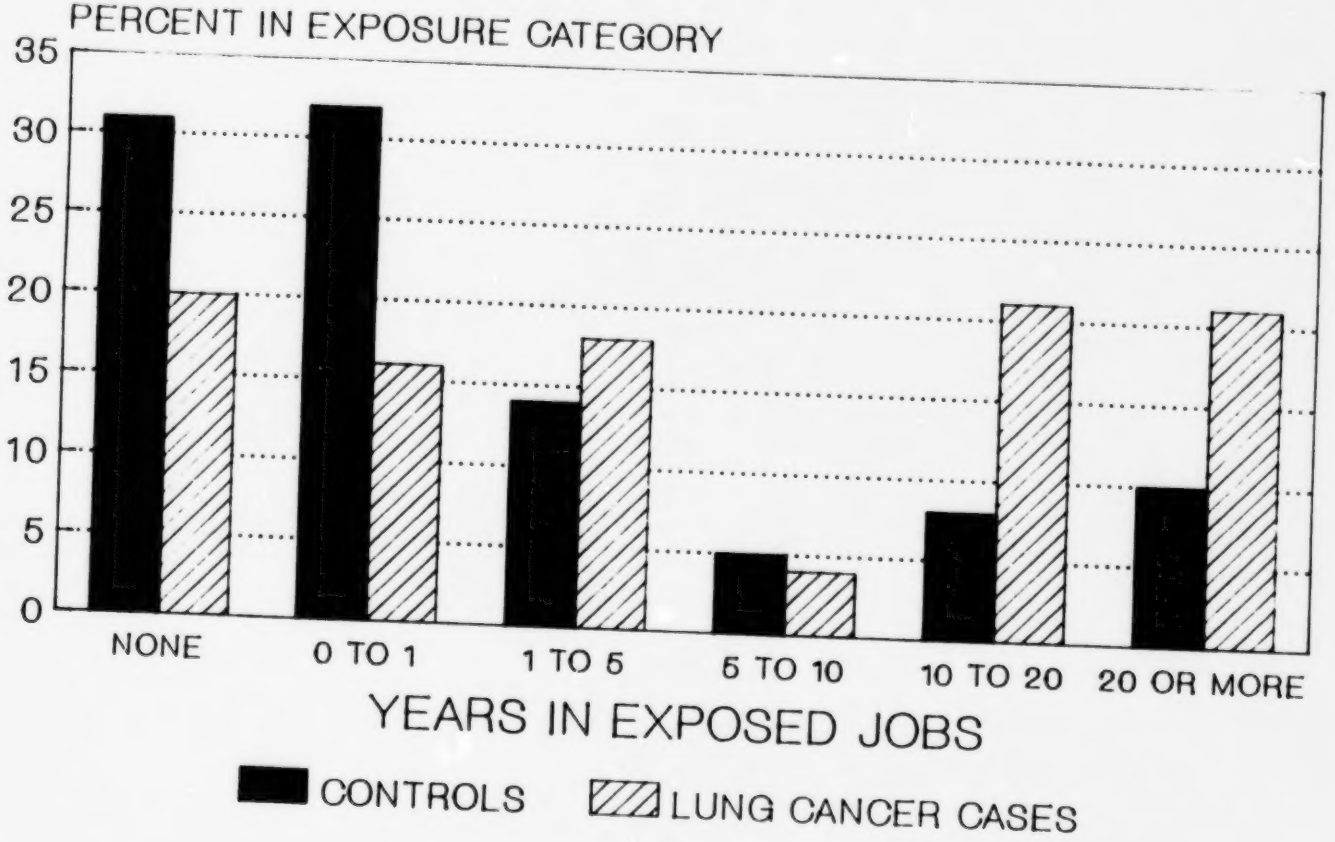


FIGURE 2

5) Latency:

For the purposes of this report, latency is defined as the length of time between hire and death. Experience has shown that asbestos is unlikely to cause death from lung cancer earlier than 10 years from first exposure, and in the Cohort Analysis, no increased risk was detectable prior to 20 years after first exposure. Table 5 gives the exposure distributions for the 56 men who died with lung cancer 20 or more years after hire, and of their matched controls.

TABLE 5

DISTRIBUTION OF EXPOSURES AMONG MEN DYING WITH LUNG CANCER 20 YEARS OR MORE AFTER HIRE

	YEARS IN EXPOSURE					
	0	< 1	1-5	5-10	10-20	> 20
CONTROLS	52	53	24	9	13	17
CASES	11	9	10	2	12	12
ALL	63	62	34	11	25	29

It can be seen that there is a clustering of lung cancer victims in the highest exposure categories; while there were 11 men (17%) with lung cancer among the 63 men who did not work in exposed jobs, there were 24 with lung cancer (44%) among the 54 who had worked in exposed jobs for 10 years or more. This data may be tested for "dose-response" with a statistical procedure known as the Chi-Square Test for Trend. The result indicates a highly significant association between the length of exposure and the risk of lung cancer, with a P-value < 0.001. The Relative Risks of Lung Cancer, comparing the men with any exposure to the group of 63 with no exposed jobs at all, are as follows:

RELATIVE RISK OF LUNG CANCER ACCORDING TO LENGTH OF EXPOSURE

YEARS IN EXPOSED JOBS	RISK RELATIVE TO THE UNEXPOSED
NO EXPOSURE	1.0
LESS THAN 1 YEAR	0.8
1 TO 5 YEARS	2.0
5 TO 10 YEARS	1.1
10 TO 20 YEARS	4.4
20 YEARS OR MORE	3.3

Because the number of individuals in any exposure category is small, from a statistical point of view, neighboring categories were amalgamated to give a more stable statistical result. Since there was no detectable risk among men with less than 1 year in exposed jobs, the reference category will consist of the combined group of "Unexposed Men and Men in Exposed Jobs for Less than 1 Year"; this category will be referred to as EXPOSED LESS THAN 1 YEAR.

For men dying 20 or more years after first employment, the risk of lung cancer, relative to those exposed for less than 1 year, is then as follows:

TABLE 6: RELATIVE RISK OF LUNG CANCER BY LENGTH OF EXPOSURE

YEARS IN EXPOSED JOBS	RISK RELATIVE TO LOWEST CATEGORY
LESS THAN 1 YEAR	1.0
1 TO 10 YEARS	1.8
10 YEARS OR MORE	4.0

Five men died with lung cancer between 15 and 20 years after hire. There was no detectable association between lung cancer risk and exposure in this group of 5 cases and 15 controls. Two cases and 8 controls had been unexposed, while 3 cases and 7 controls had been exposed for a year or longer.

6) FACTORS MODIFYING LUNG CANCER RISK

a) Age and Year of Hire

The Chi-Square analyses presented above ignore the fact that the control subjects were individually matched to their respective cases by age and year of hire. The estimates of relative risk presented above may thus be inaccurate if there is an association between either age or hire year and exposure. A more rigorous analysis takes account of the matching process and may be done in a variety of ways.

A Mantel-Haenszel stratified analysis was performed using 3 strata for Year of Hire [1: Before 1950; 2: January 1, 1950 to December 31, 1954; and 3: January 1, 1955 or later] and 3 levels of Age at Hire (19-30; 30-40; 40-50). Control for these variables did not substantially modify the unstratified estimates of risk presented in Table 6.

A Conditional Logistic Regression Analysis was performed in which each case and his 3 matches was considered to form a separate stratum in the analysis. The results are presented in Table 7.

TABLE 7: CONDITIONAL LOGISTIC REGRESSION ON LUNG CANCER RISK
TWENTY OR MORE YEARS AFTER HIRE

YEARS IN EXPOSED JOBS	RELATIVE RISK	90% CONFIDENCE LIMITS
LESS THAN 1 YEAR	1.0	
1 TO 10 YEARS	1.8	[.92, 3.6]
10 YEARS OR MORE	4.5	[2.4, 8.7]

MODEL FIT: P < 0.001

The relative risks calculated in this analysis are similar to those calculated in the unstratified analysis, again

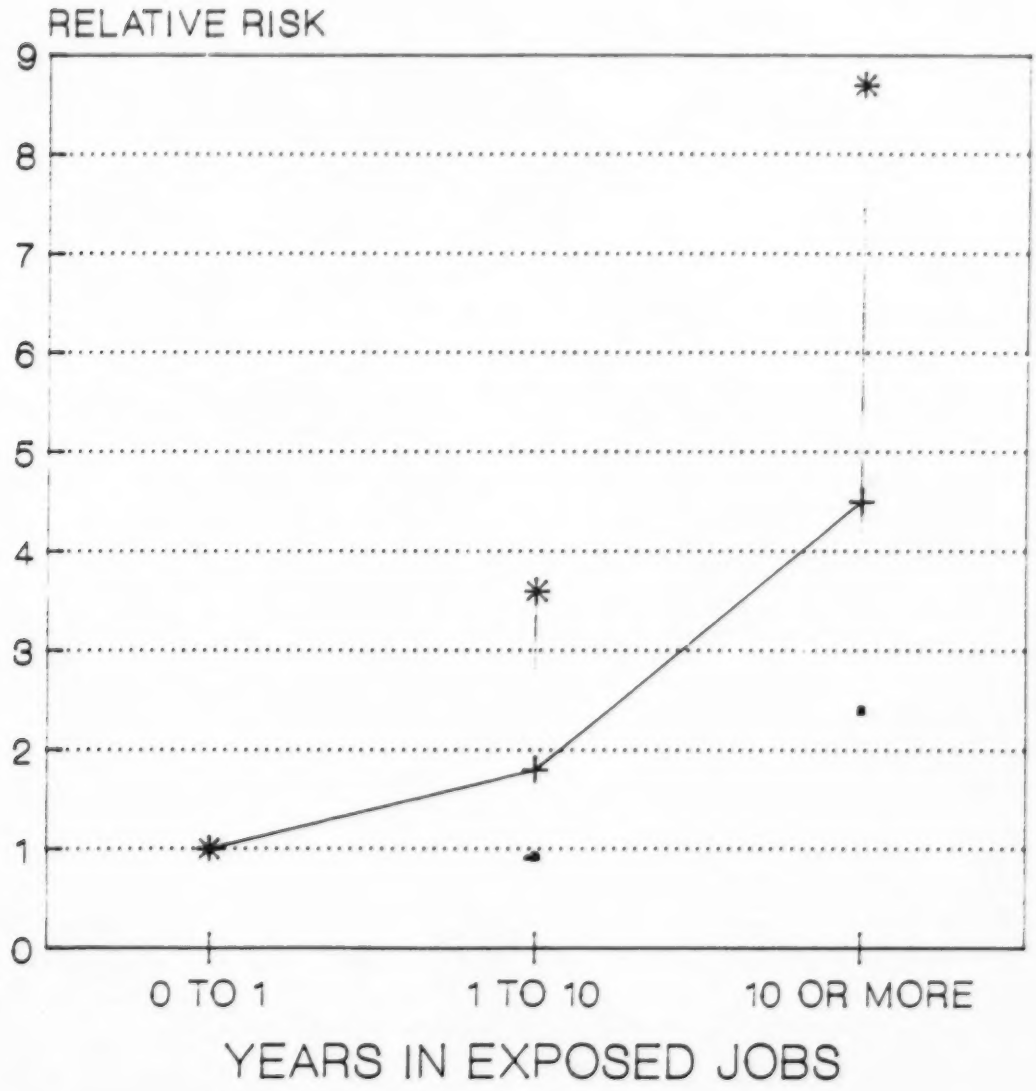
suggesting that age at hire and year of hire had very little modifying influence on lung cancer risk.

The third approach was to ignore the matching and to enter Exposure, Age, and Year of Hire independently as variables in an Unconditional Logistic Regression Analysis. To avoid the exponential dose-response form inherent in the logistic model, each variable was grouped into 3 categories, with boundaries the same as for the stratified analyses discussed previously. In this analysis, neither Age at Hire nor Year of Hire made a significant contribution to the model. Years of Exposure was significantly associated with lung cancer risk, and the results were similar to those presented above. Relative to the group of men exposed less than 1 year, the lung cancer risk was 2.0 (90% CI 1.0 - 4.2) for those exposed from 1 to 10 years and 4.8 (90% CI 2.5 - 9.0) for those exposed 10 years or more.

The relative risk calculated for the group who worked in exposure between 1 and 10 years is of borderline statistical significance in both the conditional and unconditional models. (The 2-tailed lower 90% confidence limits presented here correspond to the 95% confidence limits in a 1-tailed hypothesis test which postulates that exposure to asbestos causes rather than prevents lung cancer). It should be borne in mind that the number of cancer cases under study is so small that the statistical power to declare an increase in risk to be statistically significant is limited. To have a 90% chance of declaring a doubling of risk in the middle exposure category to be statistically significant would require a total study size of 86 cases and 258 controls. In this study there were only 56 cases and 168 controls with latencies of 20 years or more, and so this study does not have the statistical power to declare the increased risk in the middle exposure category to be statistically significant, even if the risk in this category were doubled compared to the unexposed workers.

The relationship between Years of Exposure and Relative Risk of Lung Cancer is presented graphically in Figure 3.

FIGURE 3: RELATIVE RISK OF LUNG CANCER VERSUS YEARS IN EXPOSURE



ERROR BARS GIVE 90% CONFIDENCE INTERVALS

b) Cigarette Smoking as a Risk Factor:

Cigarette smoking is recognized as an important cause of lung cancer. If the prevalence of smoking were not the same in each of the asbestos exposure categories, then the estimates of relative risk attributable to asbestos exposure might be distorted. This factor was examined in the case-control analysis.

Information about smoking habits was available from questionnaire and other sources for 31 of the lung cancer victims and 69 of the control subjects. The information was categorized as "Ever Smoked Cigarettes" or "Never Smoked Cigarettes". Thirty-one (100%) of the men with lung cancer had smoked cigarettes compared with 54 (78%) of the control subjects. The association between smoking and lung cancer is highly significant ($P < 0.01$; Fisher's Exact Test), but because no cases of lung cancer were identified in "Never Smokers" it is not possible, mathematically, to make any adjustments to the asbestos risk estimates for differences in smoking habit.

7) Gastrointestinal Cancer

There were 17 men, who died 20 or more years after hire, in whom gastrointestinal cancer was diagnosed either before death or from the examination of tissue after death. Each of these men was individually matched with 3 other members of the Johns-Manville population, using random numbers to ensure an unbiased selection process, and restricting eligibility to those potential matches who were still alive at the date of death of the case. The factors used in matching were year of birth and year of hire, and an attempt was made to match as closely as possible on these variables.

One of these deaths was from cancer of the esophagus, 8 men received the diagnosis of cancer of the stomach and 8 men were diagnosed as having bowel cancer. The distributions of exposures for the 17 men who died with gastrointestinal cancer, 20 or more years after hire, and of their 51 control subjects

is given in Table 8.

TABLE 8: THE NUMBERS OF GASTROINTESTINAL CANCER CASES AND CONTROL SUBJECTS BY YEARS SPENT IN EXPOSED JOBS

	YEARS IN EXPOSURE		
	0 TO 1	1 TO 10	10 OR MORE
CONTROLS	34	11	6
CASES	3	8	6
TOTAL	37	19	12

This Table indicates that 34 (67%) of 51 controls were exposed for less than one year, with the implication that 67% of the entire Johns-Manville population, with ages and dates of hire similar to those of the victims of gastrointestinal cancer, were exposed for less than 1 year. Since the lung cancer victims were similar in age and date of hire to the men with gastrointestinal cancer, it is interesting to compare the estimates of population exposure derived from the gastrointestinal cancer controls with those derived from the lung cancer controls (Table 5). These estimates were derived by random sampling from the Johns-Manville population and should be similar. In fact, they are. The distribution of lung cancer controls (Table 5) suggests that 63%, (105/168), of the Johns-Manville population were exposed for less than one year, compared to an estimate of 67% from the gastrointestinal cancer controls. Given this similarity in the estimates, one feels comfortable in comparing the exposure distributions of the cancer victims to those of the control subjects.

As with lung cancer, there is a clustering of men with gastrointestinal cancer in the higher exposure categories, suggesting an association between the risk of gastrointestinal cancer and asbestos exposure. This association may be tested for "dose-response" with the Chi-Square Test for Trend, and the result is highly significant, with a P-Value < 0.001. The

unmatched Relative Risks for gastrointestinal cancer, using the men who were unexposed or exposed for less than 1 year as the reference group are:

Relative Risks (Unmatched Analysis) for Gastrointestinal Cancer

YEARS IN EXPOSURE	RELATIVE RISK
UNEXPOSED OR LESS THAN 1	1.0
1 TO 10	8.2
10 OR MORE	11.3

The fact that the controls were individually matched to the cases may be taken account of in a Conditional Logistic Regression analysis which treats each case and his three matched controls as a unit in the analysis. The results are given in Table 9.

Table 9: RESULTS OF MATCHED (CONDITIONAL LOGISTIC REGRESSION) ANALYSIS FOR THE RISK OF GASTROINTESTINAL CANCER

YEARS IN EXPOSURE	RELATIVE RISK WITH 90% CONFIDENCE LIMITS
UNEXPOSED OR LESS THAN 1	1.0
1 TO 10	16.4 [2.8, 97]
10 OR MORE	34.5 [4.5, 290]

The results of the matched analysis appear quite different from those of the unmatched analysis, suggesting that there is an association between the risk of gastrointestinal cancer and age at hire or date of hire in this workforce. When, however, an Unconditional Logistic Regression Model, incorporating

Exposure, Year of Hire, and Age at Hire as variables, was analyzed neither Age nor Hire Year made statistically significant independent contributions to the model. It should be noted that we are dealing with only 17 cases of disease and the statistical results are consequently quite unstable. This may be observed directly from an examination of the 90% confidence intervals, displayed in Table 9, which are very wide in this analysis.

The risk of gastrointestinal cancer appears, at face value, to be much higher, than the risk of lung cancer, but an examination of the Confidence Intervals for the risk estimates in Tables 7 and 9 finds that they overlap. It is not unreasonable to assume that, in the Johns-Manville population, the increases in risk attributable to exposure to asbestos are similar for lung and gastrointestinal cancers. When the lung and gastrointestinal cancer subjects were combined and analyzed together in a Conditional Logistic Regression Model, the following results were obtained:

Table 10: RESULTS OF MATCHED (CONDITIONAL LOGISTIC REGRESSION) ANALYSIS FOR THE RISK OF GASTROINTESTINAL CANCER OR LUNG CANCER

YEARS IN EXPOSURE	RELATIVE RISK WITH 90% CONFIDENCE LIMITS
UNEXPOSED OR LESS THAN 1	1.0
1 TO 10	2.7 [1.5, 4.9]
10 OR MORE	5.8 [1.7, 56]

INTERPRETATION: Exposure to asbestos at the Johns-Manville factory in West Hill, Ontario was associated with an increased risk of lung and gastrointestinal cancers. Compared to workers in unexposed jobs or workers who had worked for less than 1 year in exposed jobs, men who were exposed to asbestos from 1 to 10 years had a risk of cancer that was approximately

doubled, while men who worked more than 10 years in exposed jobs had a risk of cancer that was increased approximately 5-fold.

DISCUSSION

The asbestos-induced disaster at the Johns-Manville plant in West Hill, Ontario ranks with the worst that have been recorded in the epidemiological literature on asbestos[5]. The present report updates the cancer experience of this workforce to the end of 1985.

Workers who were employed in jobs that did not involve exposure to asbestos and workers who did have exposure to asbestos but who were employed for less than one year had a cancer experience that was not substantially different from that of the general male population of Ontario. In contrast, men who worked in asbestos-exposed jobs and who were employed one year or longer experienced an overall rate of death 50% higher than that of the general population and their cancer mortality rate was tripled. There were 33 deaths due to mesothelioma, with an average shortening of life of 15 years. The lung cancer mortality rate was tripled, with an average loss of life expectancy of 9 years, while the mortality rate due to gastrointestinal cancer was doubled, with an average loss of life expectancy of 7 years. There were no deaths from laryngeal cancer in the exposed members of this workforce.

Case-control methodology was used to investigate the association between the risk of developing lung or gastrointestinal cancers and a number of potential risk factors including asbestos exposure, age at hire, and year of hire. Detailed job histories have been collected for each worker and the results of air sampling surveys have been used to calculate quantitative asbestos-exposure profiles for each worker. As a substitute for these exposure profiles, the present analysis has used the length of time in asbestos-exposed jobs as the measure of asbestos exposure. It is known that the magnitude of exposure varied from job to job and that conditions changed with time. Length of time in exposed jobs is thus only a crude measure of asbestos "dose", but a simple measure, such as this one, is probably suitable for the development of criteria for the compensation of disease developing in these workers.

The case-control analyses indicated that no increase in lung or gastrointestinal cancer risk was detectable before 20 years from first employment. Subsequently, the length of time

spent in asbestos-exposed jobs was a significant risk factor for both lung and gastrointestinal cancers. Compared to workers in unexposed jobs or workers who had worked for less than 1 year in exposed jobs, men who were exposed to asbestos from 1 to 10 years had a risk of cancer that was approximately doubled, while men who worked more than 10 years in exposed jobs had a risk of cancer that was increased approximately 5-fold.

Only one of the cancer victims in the present analysis started work after 1960. It is known that conditions at the plant were improved as the years passed, and it is probable that workers starting later than 1960 are at lower risk of cancer. It will not be possible to make an assessment of this hypothesis until a future update of this study.

Cancer victims were identified in the present analysis as a result of death from cancer or some other certified cause. It is possible that non-fatal cases of cancer occurring in this workforce were not identified. A search could be made for such individuals by linking the Johns-Manville roll of names with the records of the Ontario Cancer Treatment and Research Foundation.

Because of the risk faced by members of this workforce, it would be tempting to recommend medical surveillance in order to detect new cancers at as early a stage as possible. Regrettably, no screening procedure has been demonstrated to alter the mortality rate for mesothelioma, lung or gastrointestinal cancers. The only action, at this time, which is likely to prove beneficial is smoking cessation. In 1983, the Health Studies Service mailed, to all members of the Johns-Manville population for whom an address could be located, an advisory recommending smoking cessation as a health protection measure. <u>It is recommended that, when the results of the present study are made public, the smoking advisory be repeated and promoted.</u>

REFERENCES

1. Finkelstein MM. Asbestosis Among Long-Term Employees of an Ontario Asbestos-Cement Factory. American Review of Respiratory Disease 1982; 125:496

2. Finkelstein MM, Vingilis JJ. Radiographic Abnormalities Among Asbestos-Cement Workers: An Exposure-Response Analysis. American Review of Respiratory Disease 1984;129:17-22.

3. Finkelstein MM. Pulmonary Function in Asbestos-Cement Workers: A Dose-Response study. Br J Ind Med 1986;43:406-413.

4. Finkelstein MM. Mortality Among Employees of an Ontario Asbestos-Cement Factory. American Review of Respiratory Disease 1984;129:754-761.

5. Report of the Royal Commission on Matters of Health and Safety Arising from the Use of Asbestos in Ontario. Ontario Ministry of the Attorney General. Toronto 1984.

6. Coleman M, Douglas A, Hermon C, Peto J. Cohort Study Analysis with a Fortran Computer Program. Int J Epidemiol 1986;15:134-137.

7. Statistics Canada. Life Tables for Canada and the Provinces. Ottawa.

8. Gustafson T. True Epistat. Epistat Services. Richardson, Texas. 1987.

9. Storer B. PECAN Statistical Software. Seattle: University of Washington, Department of Biostatistics, 1983.